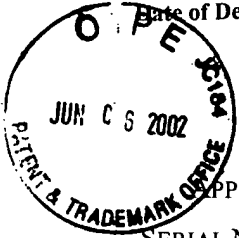


Express Mail Label: EV 074978519 US
Date of Deposit: June 6, 2002

Attorney Docket No.: 22058-531 CON

06-10-02

0360



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS : Warne, et al.

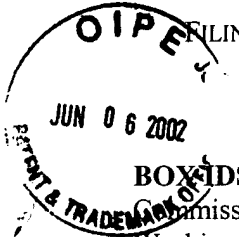
SERIAL NUMBER : 09/971,813

EXAMINER : Not Yet Assigned

FILING DATE : October 5, 2001

ART UNIT : Not Yet Assigned

FOR : FORMULATIONS FOR IL-11



BOXIDS

Commissioner for Patents
Washington, D.C. 20231



30623

PATENT TRADEMARK OFFICE

TRANSMITTAL LETTER

Transmitted herewith for filing in the present application are the following documents:

1. Information Disclosure Statement (1 page), in duplicate;
2. Modified Form 1449/PTO (4 pages), in duplicate;
3. Copies of Cited References A1-A8, B1-B2 and C1-C72; and
4. Return Postcard

If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at (617) 542-6000, Boston, Massachusetts.

The Commissioner is authorized to charge any fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311 Ref. No. 22058-531 CON. A duplicate copy of this transmittal letter is enclosed herewith.

Respectfully submitted,

Ivor R. Elufi, Reg. No. 39,529

Attorney for Applicants

MINTZ, LEVIN, COHN, FERRIS,

GLOVSKY and POPEO, P.C.

One Financial Center

Boston, Massachusetts 02111

Tel: (617) 542-6000

Fax: (617) 542-2241

Dated: June 6, 2002

Date of Deposit: June 6, 2002



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S): Warne, et al.

SERIAL NUMBER: 09/971,813

FILING DATE: October 5, 2001

FOR: *FORMULATIONS FOR IL-11*

EXAMINER: Not Yet Assigned

ART UNIT: Not Yet Assigned

BOX IDS

Commissioner for Patents
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, Applicants hereby make of record the documents listed on the attached modified Form PTO-1449 (submitted in duplicate) in the above-identified application, copies of which are submitted herewith. The order of presentation of the references should not be construed as an indication of the importance of the references.

This Information Disclosure Statement is being filed before the mailing date of a first Office Action based on the merits in the above-identified case. Accordingly, no fee or certification is believed required.

It is respectfully requested that the Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims, and signs the enclosed Form PTO-1449 to evidence that the cited information has been fully considered by the PATENT AND TRADEMARK OFFICE during the examination of this application.

Please charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311 Reference No. 22058-531CON.

Respectfully submitted,

Ivor R. Elzfi Registration No. 39,529

Attorney for the Applicants

c/o MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY and POPEO, P.C.

One Financial Center

Boston, Massachusetts 02111

Tel: (617) 542-6000

Fax: (617) 542-2241

Dated: June 6, 2002



Modified Form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Application Number	09/971,813
Filing Date	10/05/2001
First Named Inventor	Warne
Group Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	22058-531 CON

U.S. PATENT DOCUMENTS

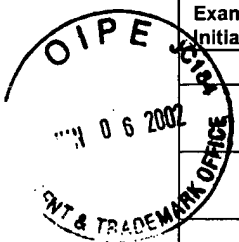
Exam Initials	Cite No.	U.S. Patent Document No.	Issue Date	Name of Patentee(s) or Applicant(s)	Class	Sub Class
	A1	5,215,895	06/01/93	Bennet, et al.		
	A2	5,270,181	12/14/93	McCoy, et al.		
	A3	5,292,646	03/08/94	McCoy, et al.		
	A4	5,679,339	10/21/97	Keith, et al.		
	A5	5,700,664	12/23/97	Yang, et al.		
	A6	5,958,401	09/28/99	Keith, et al.		
	A7	5,371,193	12/06/94	Bennett, et al.		
	A8	6,096,873	08/01/00	Schaefer, et al.		

FOREIGN PATENT DOCUMENTS

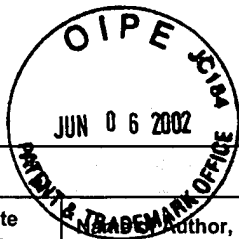
Exam Initials	Cite No.	Foreign Patent Document Office Number	Name of Patentee(s) or Applicant(s)	Date of Publication	Translation Yes	No
	B1	WO 92/04455	Genetics Institute, Inc.	03/19/1992		
	B2	WO 91/07495	Genetics Institute, Inc.	05/30/1991		

OTHER NON PATENT LITERATURE DOCUMENTS

Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C1	Siadati and Sarr.(1998). Role of extrinsic innervation in release of motilin and patterns of upper gut canine motility. <i>J. Gastrointest. Sur.</i> 2(4): 363-72.
	C2	Luiking, et al.(1998). Motilin induces gall bladder emptying and antral contractions in the fasted state in humans. <i>Gut</i> 42(6): 830-5.
	C3	Depoortere, et al. (1997). Distribution and subcellular localization of motilin binding sites in the rabbit brain. <i>Brain Res.</i> 777(1-2):103-9.
	C4	Van Assche, et al. (1997). Concentration-dependent stimulation of cholinergic motor nerves or smooth muscle by [Nle13]motilin in the isolated rabbit gastric antrum. <i>Eur. J. Pharmacol.</i> 337(2-3): 267-74.
	C5	Tomita, et al. (1997). The role of motilin and cisapride in the enteric nervous system of the lower esophageal sphincter in humans. <i>Surg. Today.</i> 27(11): 985-92.
	C6	Boivin, et al. (1997). Neural mediation of the motilin motor effect on the human antrum. <i>Am. J. Physiol.</i> 272(1 Pt 1): G71-6.
	C7	Yokoyama, et al. (1995). Recovery of gastrointestinal motility from post-operative ileus in dogs: effects of Leu13-motilin (KW-5139) and prostaglandin F2 alpha. <i>Neurogastroenterol. Motil.</i> 7(4): 199-210.
	C8	De Clercq, et al. (1998). Motilin in human milk: identification and stability during digestion. <i>Life Sci.</i> 63(22): 1993-2000.
	C9	Ordaz-Jimenez, et al. (1998). [Gastrointestinal hormones during minimal enteral feeding of sick premature infants] <i>Rev. Invest. Clin.</i> 50(1): 37-42. (Spanish w/ English abstract).
	C10	Jadcherla, et al. (1997). Regulation of migrating motor complexes by motilin and pancreatic

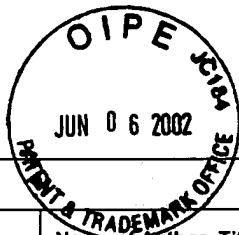


OTHER NON PATENT LITERATURE DOCUMENTS		
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
		polypeptide in human infants. <i>Pediatr. Res.</i> <u>42</u> (3): 365-9.
	C11	Omura , et al. (1987). Macrolides with gastrointestinal motor stimulating activity. <i>J Med Chem.</i> <u>30</u> (11): 1941-3.
	C12	Weich, et al (1997). Recombinant human interleukin-11 directly promotes megakaryocytopoiesis in vitro. <i>Blood.</i> <u>90</u> (10): 3893-902.
	C13	Orazi , et al. (1996). Effects of recombinant human interleukin-11 (Neumega rhIL-11 growth factor) on megakaryocytopoiesis in human bone marrow. <i>Exp. Hematol.</i> <u>24</u> (11): 1289-97.
	C14	Du, et al. (1997). Protective effects of interleukin-11 in a murine model of ischemic bowel necrosis. <i>Am. J. Physiol.</i> <u>272</u> (3 Pt 1): G545-52.
	C15	Orazi , et al. (1996). Interleukin-11 prevents apoptosis and accelerates recovery of small intestinal mucosa in mice treated with combined chemotherapy and radiation. <i>Lab. Invest.</i> <u>75</u> (1): 33-42.
	C16	Keith, et al. (1994). "IL-11, a pleiotropic cytokine: exciting new effects of IL-11 on gastrointestinal mucosal biology." <i>Stem Cells.</i> <u>12</u> (Suppl 1):79-90.
	C17	Qiu, et al.. (1996). Protection by recombinant human interleukin-11 against experimental TNB-induced colitis in rats. <i>Dig. Dis. Sci.</i> <u>41</u> (8): 1625-30.
	C18	Hill, et al. (1998). Interleukin-11 promotes T cell polarization and prevents acute graft-versus-host disease after allogeneic bone marrow transplantation. <i>J. Clin. Invest.</i> <u>102</u> (1): 115-23.
	C19	Redlich, et al. (1996). IL-11 enhances survival and decreases TNF production after radiation-induced thoracic injury. <i>J. Immunol.</i> <u>157</u> (4): 1705-10.
	C20	Waxman , et al. (1998). Targeted lung expression of interleukin-11 enhances murine tolerance of 100% oxygen and diminishes hyperoxia-induced DNA fragmentation. <i>J Clin Invest.</i> <u>101</u> (9):1970-82.
	C21	Leng and Elias (1997). Interleukin-11 inhibits macrophage interleukin-12 production. <i>J. Immunol.</i> <u>159</u> (5): 2161-8.
	C22	Trepicchio, et al. (1997). IL-11 regulates macrophage effector function through the inhibition of nuclear factor-kappaB. <i>J. Immunol.</i> <u>159</u> (11): 5661-70.
	C23	Trepicchio, et al. (1996). Recombinant human IL-11 attenuates the inflammatory response through down-regulation of proinflammatory cytokine release and nitric oxide production. <i>J. Immunol.</i> <u>157</u> (8): 3627-34.
	C24	Taga and Kishimoto (1997). Gp130 and the interleukin-6 family of cytokines. <i>Annu. Rev. Immunol.</i> <u>15</u> :797-819.
	C25	Zhang, et al. (1994). Ciliary neurotropic factor, interleukin 11, leukemia inhibitory factor, and oncostatin M are growth factors for human myeloma cell lines using the interleukin 6 signal transducer gp130. <i>J. Exp. Med.</i> <u>179</u> (4):1337-42.
	C26	Yang and Yin. (1995). Interleukin (IL)-11--mediated signal transduction. <i>Ann. NY Acad. Sci.</i> <u>762</u> : 31-41.
	C27	Nandurkar, et al. (1996). The human IL-11 receptor requires gp130 for signalling: demonstration by molecular cloning of the receptor. <i>Oncogene.</i> <u>12</u> (3):585-93.
	C28	Miyatake, et al. (1998). Complement-fixing elicited antibodies are a major component in the pathogenesis of xenograft rejection. <i>J. Immunol.</i> <u>160</u> (8): 4114-23
	C29	Yin, et al. (1994). Identification of a 130-kilodalton tyrosine-phosphorylated protein induced by interleukin-11 as JAK2 tyrosine kinase, which associates with gp130 signal transducer. <i>Exp. Hematol.</i> <u>22</u> (5): 467-72.
	C30	Wang, et al. (1995). Interleukin-11 induces complex formation of Grb2, Fyn, and JAK2 in 3T3L1 cells. <i>J. Biol. Chem.</i> <u>270</u> (47): 27999-8002.
	C31	Lutticken, et al. (1994). Association of transcription factor APRF and protein kinase Jak1 with the interleukin-6 signal transducer gp130. <i>Science</i> <u>263</u> (5143): 89-92.
	C32	Hemann, et al. (1996). Differential activation of acute phase response factor/Stat3 and Stat1 via the cytoplasmic domain of the interleukin 6 signal transducer gp130. <i>J. Biol. Chem.</i> <u>271</u> (22): 12999-3007.



OTHER NON PATENT LITERATURE DOCUMENTS

Exam Initials	Cite No.	Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C33	Zhong, et al. (1994). Stat3: a STAT family member activated by tyrosine phosphorylation in response to epidermal growth factor and interleukin-6. <i>Science</i> . 264(5155): 95-8
	C34	Akira (1997). IL-6-regulated transcription factors. <i>Int. J. Biochem. Cell Biol.</i> 29(12):1401-18.
	C35	Zhang, et al. (1995). Requirement of serine phosphorylation for formation of STAT-promoter complexes. <i>Science</i> 267(5206): 1990-4.
	C36	Boulton, et al. (1995). STAT3 activation by cytokines utilizing gp130 and related transducers involves a secondary modification requiring an H7-sensitive kinase. <i>Proc. Natl. Acad. Sci. USA</i> . 92(15): 6915-9.
	C37	Adunyah, et al. (1995). Interleukin-11 induces tyrosine phosphorylation, and c-jun and c-fos mRNA expression in human K562 and U937 cells. <i>Ann. NY Acad. Sci.</i> 766: 296-9.
	C38	Yin and Yang (1994). Mitogen-activated protein kinases and ribosomal S6 protein kinases are involved in signaling pathways shared by interleukin-11, interleukin-6, leukemia inhibitory factor, and oncostatin M in mouse 3T3-L1 cells. <i>J. Biol. Chem.</i> 269(5): 3731-8.
	C39	Paul, et al. (1990). Molecular cloning of a cDNA encoding interleukin 11, a stromal cell-derived lymphopoietic and hematopoietic cytokine. <i>Proc. Natl. Acad. Sci. USA</i> . 87(19):7512-6.
	C40	Balkwill and Burke (1989). The cytokine network. <i>Immunol Today</i> 10(9): 299-304.
	C41	Wong and Clark (1988). Multiple actions of interleukin 6 within a cytokine network. <i>Immunol. Today</i> . (5): 137-9.
	C42	Clark and Kamen (1987). The human hematopoietic colony-stimulating factors. <i>Science</i> . 236(4806): 1229-37.
	C43	Jacobs, et al. (1970). Characteristics of a human diploid cell designated MRC-5. <i>Nature</i> 227(254): 168-70.
	C44	Ikebuchi, et al. (1988). Synergistic factors for stem cell proliferation: further studies of the target stem cells and the mechanism of stimulation by interleukin-1, interleukin-6, and granulocyte colony-stimulating factor. <i>Blood</i> 72(6): 2007-14.
	C45	Bruno, et al. (1991). Effects of recombinant interleukin 11 on human megakaryocyte progenitor cells. <i>Exp. Hematol.</i> 19(5): 378-81.
	C46	Du and Williams (1994). Interleukin-11: a multifunctional growth factor derived from the hematopoietic microenvironment. <i>Blood</i> . 83(8): 2023-30.
	C47	Yin, et al.. (1992). Enhancement of in vitro and in vivo antigen-specific antibody responses by interleukin 11. <i>J. Exp. Med.</i> 175(1): 211-6.
	C48	Barton, et al. (1996). Interleukins 6 and 11 protect mice from mortality in a staphylococcal enterotoxin-induced toxic shock model. <i>Infect. Immun.</i> 64(3):714-8.
	C49	Castagliuolo, et al. (1997). IL-11 inhibits Clostridium difficile toxin A enterotoxicity in rat ileum. <i>Am. J. Physiol.</i> 273(2 Pt 1): G333-41.
	C50	Liu, et al. (1996). Trophic effects of interleukin-11 in rats with experimental short bowel syndrome. <i>J. Pediatr. Surg.</i> 31(8): 1047-51.
	C51	Fiore, et al. (1998). Comparison of interleukin-11 and epidermal growth factor on residual small intestine after massive small bowel resection. <i>J. Pediatr. Surg.</i> 33(1): 24-9.
	C52	Schindel, et al. (1997). Interleukin-11 improves survival and reduces bacterial translocation and bone marrow suppression in burned mice. <i>J. Pediatr. Surg.</i> 32(2): 312-5.
	C53	Musashi, et al. (1991). Synergistic interactions between interleukin-11 and interleukin-4 in support of proliferation of primitive hematopoietic progenitors of mice. <i>Blood</i> . 78(6): 1448-51.
	C54	Burstein, et al. (1992). Leukemia inhibitory factor and interleukin-11 promote maturation of murine and human megakaryocytes in vitro. <i>J. Cell. Physiol.</i> 153(2): 305-12.
	C55	Baumann and Schendel. (1991). Interleukin-11 regulates the hepatic expression of the same plasma protein genes as interleukin-6. <i>J. Biol. Chem.</i> 266(30): 20424-7.
	C56	Kawashima, et al. (1991). Molecular cloning of cDNA encoding adipogenesis inhibitory factor and



OTHER NON PATENT LITERATURE DOCUMENTS

Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
		identity with interleukin-11. <i>FEBS Lett.</i> <u>283</u> (2): 199-202.
	C57	Fann and Patterson. (1994). Neuropoietic cytokines and activin A differentially regulate the phenotype of cultured sympathetic neurons. <i>Proc. Natl. Acad. Sci. USA.</i> <u>91</u> (1): 43-7.
	C58	Yin, et al. (1993). Involvement of IL-6 signal transducer gp130 in IL-11-mediated signal transduction. <i>J. Immunol.</i> <u>151</u> (5): 2555-61.
	C59	Hibi, et al. (1990). Molecular cloning and expression of an IL-6 signal transducer, gp130. <i>Cell</i> <u>63</u> (6): 1149-57.
	C60	Omura, et al. (1985). Gastrointestinal motor-stimulating activity of macrolide antibiotics and the structure-activity relationship. <i>J. Antibiot. (Tokyo)</i> <u>38</u> (11) : 1631-2.
	C61	Depoortere, et al. (1998). <i>Am. Gastroenterology Soc.</i> (New Orleans, LA, May 16-22, 1998).
	C62	Opal, et al. (1998). Recombinant human interleukin-11 in experimental <i>Pseudomonas aeruginosa</i> sepsis in immunocompromised animals. <i>J. Infect. Dis.</i> <u>178</u> (4) : 1205-8.
	C63	Girasole, et al. (1994). Interleukin-11: a new cytokine critical for osteoclast development. <i>J. Clin. Invest.</i> <u>93</u> (4):1516-24.
	C64	Keith, et al. (1995). <i>Gastroenterology</i> <u>108</u> (4): A846.
	C65	Keith, et al. (1994). <i>Gastroenterology</i> <u>106</u> (4 part 2): A708.
	C66	Opal, et al. (1995). <i>Blood</i> <u>86</u> (10): 498A.
	C67	Sonis, et al. (1995). Alteration in the frequency, severity and duration of chemotherapy-induced mucositis in hamsters by interleukin-11. <i>Eur. J. Cancer B. Oral Oncol.</i> <u>31B</u> (4): 261-6.
	C68	Leonard, et al. (1995). Prevention of experimental autoimmune encephalomyelitis by antibodies against interleukin 12. <i>J. Exp. Med.</i> <u>181</u> (1): 381-6.
	C69	Scofield, et al. (1993). A hypothesis for the HLA-B27 immune dysregulation in spondyloarthritis: contributions from enteric organisms, B27 structure, peptides bound by B27, and convergent evolution. <i>Proc. Natl. Acad. Sci. USA.</i> <u>90</u> (20): 9330-4.
	C70	Hammer, et al. (1990). Spontaneous inflammatory disease in transgenic rats expressing HLA-B27 and human beta 2m: an animal model of HLA-B27-associated human disorders. <i>Cell.</i> <u>63</u> (5): 1099-112.
	C71	Sonis, et al. (1995). <i>Proc. Am. Assoc. Cancer Res.</i> <u>36</u> : 368.
	C72	Remington (1995). <i>The Science and Practice of Pharmacy</i> Volume 2: 1403-1404 and 1626-1627. (Mack Publishing – 19 th edition).

* a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, U.S.S.N. _____, filed _____, and relied upon for an earlier filing date under 35 U.S.C. §120 (continuation, continuation-in-part, and divisional applications).

Examiner Signature		Date Considered	
--------------------	--	-----------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered.

Include copy of this form with next communication to applicant.